

REMARKS

The claims have been amended simply to conform to U.S. practice and eliminate multiple dependencies to reduce fees. No new matter has been added and entry of the amendment is respectfully requested.

Enclosed is the following Exhibit A: Marked-up Version of Amendments to the Specification and Claims.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 246152015600.

Respectfully submitted,

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EXHIBIT A: - VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

1. A polynucleotide comprising:
 - (i) a nucleic acid sequence set out in SEQ. ID. NO: 5, 7 or 9 or a sequence complementary thereto; or
 - (ii) a homologue or fragment of a sequence defined in (i).
2. A polynucleotide according to claim 1 consisting essentially of the nucleic acid sequence set out in SEQ ID NO: 5, 7 or 9 or a sequence complementary thereto.
3. (Amended) A polypeptide encoded by a polynucleotide according to claim 1 [or 2].
4. (Amended) A polypeptide obtainable by expressing a polynucleotide according to claim 1 [or 2] in a cell which is a *Streptomyces* cell or a cell of a heterologous species.
5. A polypeptide comprising the amino acid sequence set out in SEQ ID NO: 6, 8 or 9 or a homologue or fragment thereof.
6. (Amended) A recombinant cell comprising at least one additional copy of a polynucleotide according to claim 1 [or 2], wherein the cell naturally possesses at least one said polynucleotide.
7. A recombinant cell according to claim 6, wherein the cell is one which naturally produces pimarinin or a related molecule.
8. A recombinant cell according to claim 7 which is a *Streptomyces natalensis* cell.
9. (Amended) A recombinant cell, wherein a polynucleotide according to claim 1 [or 2] which naturally occurs in the cell has been inactivated.

10. A recombinant cell according to claim 9, wherein the cell is one which naturally produces pimarinin or a related molecule.

11. A recombinant cell according to claim 10 which is a *Streptomyces natalensis* cell.

12. (Amended) A recombinant cell comprising a polynucleotide according to claim 1 [or 2] which polynucleotide does not naturally occur in that cell or where the polynucleotide is heterologous to that cell.

13. A recombinant cell according to claim 12, wherein the cell is one which does not naturally produce pimarinin.

14. A recombinant cell according to claim 13 which is a *Streptomyces lividans* or *Streptomyces coelicolor* cell.

15. (Amended) A method for overexpressing a polynucleotide encoding a polypeptide according to [any one of claims 3 to 5] claim 5 in a *Streptomyces* cell which method comprises:

- (i) attaching a promoter sequence to the said polynucleotide;
- (ii) transferring the resulting promoter-polynucleotide complex into the said cell; and
- (iii) maintaining the resulting cell under conditions suitable for expression of the said polynucleotide.

16. (Amended) A method for inactivating a polynucleotide encoding a polypeptide according to [any one of claims 3 to 5] claim 5 in a *Streptomyces* cell which method comprises disrupting the coding sequence of the said polynucleotide.

17. (Amended) A method for expressing a polynucleotide encoding a polypeptide according to [any one of claims 3 to 5] claim 5 in a heterologous cell which method comprises:

- (i) attaching a promoter sequence to the said polynucleotide;
- (ii) transferring the resulting promoter-polynucleotide complex into the said cell; and

(iii) maintaining the resulting cell under conditions suitable for expression of the said polynucleotide.

18. (Amended) A method for producing pimaricin which method comprises maintaining a cell according to [any one of claims 6 to 8] claim 6 under conditions suitable for obtaining expression of [the] said additional copy of a polynucleotide [according to claim 1 or 2] and isolating [the said] pimaricin.

19. (Amended) A method for producing a biomolecule which method comprises maintaining a cell according to [any one of claims 9 to 11] claim 9 under conditions which would be suitable for obtaining expression of the inactivated polynucleotide had it not been inactivated and isolating [the] said biomolecule.

20. (Amended) A method for producing a biomolecule which method comprises maintaining a cell according to [any one of claims 12 to 14] claim 12 under conditions suitable for obtaining expression of [the] said polynucleotide [which does not naturally occur in the cell] and isolating [the] said biomolecule.

21. (Amended) A biomolecule obtainable by a method according to claim 19[or 20].

24. (Amended) A vector containing a polynucleotide according to claim 1 [or 2] which is capable of expressing a polypeptide [according to any one of claims 3 to 5] encoded by said polynucleotide.

25. (Amended) A cell [harbouring] comprising a vector according to claim 24.

26. (Amended) A method for producing a polypeptide [according to any one of claims 3 to 5] comprising the amino acid sequence set out in SEQ ID NO: 6, 8 or 9 or a homologue or fragment thereof, which method comprises maintaining a cell according to claim 25 under conditions suitable for obtaining expression of the polypeptide and isolating the said polypeptide.

27. (Amended) [Use of] A method to oxidize a methyl group contained in a compound which method comprises contacting said compound with an isolated or purified polypeptide according to [any one of claims 3 to 5] claim 5 [for the oxidative modification of a methylgroup of a suitable compound].